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Focusing the Power of NextGen Sequencing on Navy Medicine

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Genomics and bioinformatics are two intertwined and constantly changing fields affecting the way we live. The idea of having your genome sequenced, and maybe even downloaded to your smartphone, is now a very real and attainable possibility, and not the stuff of science fiction.

We have reached the age when parents of children with very unique disorders have their genomes sequenced, when acts of bioterrorism are investigated using genomic evidence, and when the idea of extending sequencing capacity into the field is becoming more and more plausible. Pathogens are routinely discovered through nextgen sequencing of patient samples and the idea of using sequencers routinely for diagnostics in clinical laboratories is being widely considered.

In the Biological Defense Research Directorate (BDRD) Genomics Department at the Naval Medical Research Center our colleagues are engaged in some very exciting, cutting edge research ranging from sequencing bat genomes or uncovering clues leading to the design of novel antiviral drugs to analyzing pathogen genomes to create vaccines and detection assays.

On any given day our team is focusing on classic biowarfare pathogens with an obvious connection to biological defense to examining areas with the potential to impact the health and wellbeing of our sailors and Marines and their families. Despite the many ongoing research projects in our laboratory, one thing remains a constant – the ever-changing technologies we use to do this research.

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The technology is improving at such a pace that a $10,000 genome is quickly replaced by a $1,000 genome and that by a $500 genome and so on. And the software used in the sequencing instruments improves so throughput increases and data production costs decrease and the production of several gigabyte sized datasets can be done by one person in a day.

We are excited by all these technological advancements! We can't help but be excited by how far we've come so quickly and the creative possibilities that lie ahead to do amazing things with these technologies. The instruments at our disposal are enormous data creators. They are very powerful but also limited in how the researcher designs an experiment. We still have to take pains to ensure the right controls are included and the sample collection and preparation is performed in such a way as to not bias the results.

Since this is such a rapidly evolving science, there is some basic groundwork to be laid and challenges met to ensure success in deploying these sequencers in environments such as the clinic or the field. When we are working with complex samples, such as a stool sample or a handful of soil, there are so many different microorganisms present that a given pathogen of interest may constitute less than one percent of the total sample. While it is fairly commonplace and accepted to detect or discover an organism based on one or two specific DNA fragments found out of 100,000 or more, we still need to figure out how many times to run the sample through the sequencers in order to *exclude* the presence of a specific microorganism. Investigating fundamental questions such as this one is key to our ability to be able to employ these technologies to their fullest potential to support Navy Medicine.

Although we are on the cusp of great things in applying genomics to Navy Medicine and biodefense, we realized it behooves us to temper our excitement about diving into real world samples to see what we can find in them, and to approach these problems as a proper science experiment. All eyes are on genomics and the stakes are getting high, with people considering how best to use genomic data and the time has come to dig in and determine what the characteristics and limitations of these sequencing platforms and analytical methods really are, so the data will be interpreted correctly.

For our group this is quite an active and satisfying area of research. For the past several years we have been creating artificial samples to mimic human clinical samples or environmental samples, and using these artificial samples to test different sequencing platforms for their sensitivity, specificity, reproducibility, etc. The benefit of systematically sampling from artificial samples is that we know how many microorganisms these samples contain which allows us to compare our sequencing results from the multiple different platforms or sample preparation methods and draw conclusions about detection and discrimination. Through these efforts, we believe that we will gain a better understanding of what is possible and realistic in the clinic, in the field, and elsewhere, and how best to employ these technologies for the benefit of Navy medicine and public health.

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